



## Clinical trial results:

**An open-label, multi-national, multi-center, single-arm, uncontrolled, longterm extension study of orally administered riociguat in patients with symptomatic pulmonary arterial hypertension (PAH) who received riociguat in a Bayer clinical trial**

### Summary

EudraCT number	2016-000501-36
Trial protocol	FR IT
Global end of trial date	15 September 2025

### Results information

Result version number	v1 (current)
This version publication date	27 February 2026
First version publication date	27 February 2026

### Trial information

#### Trial identification

Sponsor protocol code	BAY63-2521/18694
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#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02759419
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser Wilhelm Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, +49 30 300139003, clinical-trials-contact@bayer.com

Notes:

### Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 October 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 September 2025
Global end of trial reached?	Yes
Global end of trial date	15 September 2025
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

To provide riociguat therapy to eligible patients with PAH originating from the Bayer-sponsored trials 12935 PATENT-2 or 16719 RESPITE who are currently or recently treated in these trials until lack of patient benefit as assessed by investigator, or commercial availability and reimbursement.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent was read by and explained to all the subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Korea, Republic of: 11
Worldwide total number of subjects	18
EEA total number of subjects	7

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0

Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	15
From 65 to 84 years	3
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at 9 study centers in 2 countries (5 in France and 4 in South Korea) between 16 June 2016 (first participant first visit) consent) and 15 September 2025 (last participant last visit).

### Pre-assignment

Screening details:

A total of 18 participants were enrolled and no participant failed screening.

All 18 participants received study intervention. 12 Participants did not complete the treatment phase.

### Period 1

Period 1 title	overall (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	Riociguat (BAY 63-2521)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Riociguat (BAY 63-2521)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

0.5 to 2.5 mg in 0.5 mg increments (according to individually adapted optimal dose) administered three times daily

Number of subjects in period 1	Riociguat (BAY 63-2521)
Started	18
Completed	6
Not completed	12
Consent withdrawn by subject	1
Physician decision	5
Adverse event, non-fatal	1
Death	4
Lost to follow-up	1

## Baseline characteristics

### Reporting groups

Reporting group title	Riociguat (BAY 63-2521)
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Reporting group description: -

Reporting group values	Riociguat (BAY 63-2521)	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	15	15	
From 65-84 years	3	3	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	12	12	
Male	6	6	

## End points

### End points reporting groups

Reporting group title	Riociguat (BAY 63-2521)
Reporting group description: -	

### Primary: Number of Participants with treatment emergent adverse events (TEAE)s

End point title	Number of Participants with treatment emergent adverse events (TEAE)s <sup>[1]</sup>
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End point description:

End point type	Primary
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End point timeframe:

From first intake of study medication until end of study.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Due to the limited number of patients, statistical analyses included in this study focused on descriptive statistics only.

End point values	Riociguat (BAY 63-2521)			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Participants				
any TEAE	18			
mild TEAE	3			
moderate TEAE	6			
severe TEAE	9			
any treatment-related TEAE	5			
mild treatment-related TEAE	2			
moderate treatment-related TEAE	2			
severe treatment-related TEAE	1			
any TEAE leading to discontinuation of intervention	5			
any TEAE leading to modification of intervention	0			
any TEAE of special interest	0			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse event data were collected after signing the informed consent until 30 days after end of study treatment over a period of approximately five years.

Adverse event reporting additional description:

12 participants (66.7%) reported at least 1 treatment-emergent SAE (cross ref to table) including 4 deaths. None of the treatment emergent SAE/death was assessed as treatment-related.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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### Reporting groups

Reporting group title	Full Analysis Set
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Reporting group description:

All 18 participants, who have been included in the study and have received at least one dose of the study treatment.

Serious adverse events	Full Analysis Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 18 (66.67%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm recurrence			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Bleeding varicose vein			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			

Peritoneal catheter insertion			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salpingo-oophorectomy bilateral			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pulmonary arterial hypertension			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Lung disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial flutter			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			



subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Palpitations			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Right ventricular failure			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic encephalopathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vocal cord paralysis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombotic microangiopathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haemoperitoneum			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Bile duct stenosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hepatic cirrhosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Proteinuria			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

<b>Non-serious adverse events</b>	Full Analysis Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)		
Vascular disorders			
Bleeding varicose vein			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Surgical and medical procedures			
Liver transplant			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
General disorders and administration site conditions			
Administration site pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Chest pain			

subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Fatigue			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Oedema			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	5		
Pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Inflammation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Pelvic cyst			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vaginal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	5		
Epistaxis			

subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Lung disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Orthopnoea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pulmonary arterial hypertension			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Sleep apnoea syndrome			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Snoring			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Product issues			
Device breakage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Investigations			
N-terminal prohormone brain natriuretic peptide increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Platelet count decreased			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)  Ligament sprain subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1  1 / 18 (5.56%) 1		
Cardiac disorders Arrhythmia subjects affected / exposed occurrences (all)  Atrial fibrillation subjects affected / exposed occurrences (all)  Right ventricular failure subjects affected / exposed occurrences (all)  Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1  2 / 18 (11.11%) 2  2 / 18 (11.11%) 3  1 / 18 (5.56%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)  Essential tremor subjects affected / exposed occurrences (all)  Headache subjects affected / exposed occurrences (all)  Presyncope subjects affected / exposed occurrences (all)  Syncope	3 / 18 (16.67%) 6  1 / 18 (5.56%) 1  6 / 18 (33.33%) 7  1 / 18 (5.56%) 1		

subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Thrombocytopenia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eye disorders			
Cataract			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diabetic retinopathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Glaucoma			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Macular degeneration			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Conjunctival oedema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	4		
Abdominal pain upper			



subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Ascites			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	7 / 18 (38.89%)		
occurrences (all)	11		
Functional gastrointestinal disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastric ulcer			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Haematemesis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Haematochezia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Melaena			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	3		
Oesophagitis			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Small intestinal haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Tooth disorder			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Hepatobiliary disorders			
Bile duct stenosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	3		
Cholangitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Congestive hepatopathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Skin reaction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Renal and urinary disorders			

Acute kidney injury subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Chronic kidney disease subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Back pain subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3		
Coccydynia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Myalgia subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Pain in extremity subjects affected / exposed occurrences (all)	3 / 18 (16.67%) 3		
Pain in jaw subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Torticollis subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Infections and infestations			

COVID-19			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	4		
Cellulitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ear infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Erysipelas			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Fungal infection			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastroenteritis			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Influenza			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Otitis externa			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rhinitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		

Septic shock subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Metabolism and nutrition disorders			
Dehydration subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Folate deficiency subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Gout subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Iron deficiency subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 August 2016	inclusion of a new exclusion criterion
10 March 2017	Opening of the study for patients from study 18588 (REPLACE)

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported